DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Central Region

Food and Drug Administration
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone (973) 526-6006

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CERTIFIED MAIL
RETURN RECEIPT REQUESTED

March 20, 2001

WARNING LETTER

Mr. Terrance Fortino
President and Chief Executive Officer
Mid-Atlantic Diagnostics
338 Stokes Road Suite E
Medford, NJ 08055

FILE NO: 01-NWJ-20

Dear Mr. Fortino:

During an inspection of your firm located at the above address on February 12,13,14, and 26, 2001, our investigator determined that your firm manufactures "The Stripper", a micropipette with tips used in the manipulation and transfer of oocytes and embryos during IVF and ICSI. This product is a medical device as defined by Section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act).

The above stated inspection revealed that your micropipettes and tips are adulterated within the meaning of section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packaging, storage, or installation are not in conformance with the Quality System Regulation (QSR) for medical devices as set forth in Title 21, Code of Federal Regulations (CFR) Part 820 as follows:

1. **Your Management with executive responsibility failed to ensure that an adequate quality system has been established and maintained as required by 21 CFR 820.20. For example**:

   a. Your firm failed to conduct management review meetings that include a review of the suitability and effectiveness of the quality system.

   b. Your firm failed to conduct internal quality audits.

   c. Your firm failed to establish design control procedures, complaint procedures, and medical device reporting (MDR) procedures.

2. **Your firm failed to assure the sterility of lot 27800 which was contract sterilized by [redacted] under run 0118 at a dose less than the validated dose. For example:**

   a. According to the [redacted] Certificate of Processing dated 9/6/00, 1 box of lot 27800 was sterilized with a minimum dose of 16.3 kGy and a maximum dose of 19.1 kGy. Your current validation for this product, performed in May 2000, specifies a minimum dose of [redacted] kGy.

   b. This lot subsequently failed sterility testing performed by [redacted] and was reported on analytical test report [redacted] Ref. 0025206/2 dated 9/26/00. Although new samples were tested and found to be sterile on analytical test report [redacted] Ref. 0027101/1 dated 10/11/2000, there was no evidence that the original sterility failure was investigated.

   c. Your firm failed to adequately investigate the root cause of corrective action number 7 dated 9/27/00 in which the customer complained of a mouse-embryo test failure of lot 27800.

3. **Your firm failed to adequately investigate a test result from [redacted], a contract laboratory, which indicated a mouse-embryo failure for lot 09200. This test was actually a retest of lot 09200 in response to a complaint of a mouse-embryo failure (documented in your files as Corrective Action #6).**

4. **Your firm failed to investigate the root cause of a packaging integrity test failure. One of ten samples of lot 06300 sterile run 43173 failed the package integrity test (environmental and microbial challenge) in April 2000 as documented on the [redacted] Report Number H0D001 dated 6/26/00.**

5. **Your firm failed to follow your current sterilization protocol for Lots 25700, 21300, and 17400. Your validation package supports a specification of a minimum of [redacted] kGy; however these lots were sterilized below [redacted] kGy.**

6. **Your firm failed to adequately review test data sheets from your contract laboratory. For example:**

   a. Your firm failed to recognize the word "retest" on [redacted] Report for lot 27800 irradiation run 0118 ([redacted] Ref. #0027101/1) indicating a previous sterility failure. Your firm also failed to recognize that the negative controls were reported as positive and that the test data sheet did not identify results of positive controls.

   b. Your firm failed to recognize that the negative controls in the sterility test reports from [redacted] for lot 25700 run 0117, lot 32100 run 0120, and lot 27800 run 0119 were reported as positive and that the test data sheets did not identify results of positive controls.

c. Your firm failed to recognize that the sterility test report from [redacted] for lot 04501 run 0124 ([redacted] ref. #0101203/1) was marked as "preliminary release" and that the negative controls were reported as positive.

7. **Your firm failed to assure that the test method used by your contract laboratory, [redacted], is validated for your product.**

8. **Your firm failed to conduct full finished product testing on lot 27800 run 0119. This lot was resterilized on 9/30/00. Although this lot was sent for sterility testing on 10/30/00, there was no mouse-embryo testing or endotoxin testing performed. This lot was also released on 10/11/00 before the results of the sterility test were received.**

9. **Your firm distributed lot 21300 from 8/1/00 to 8/10/00 prior to completion of sterility testing. According to statements from you, [redacted] test data sheet Ref. #0020710/1 represents sterility testing for lot 21300 although it is marked with lot 17400. This data sheet shows that sterility testing wasn't completed until August 10, 2000.**

10. **There is no assurance that your product, the "Stripper", is stable for its' expiration date of two years. There were no mouse-embryo tests or endotoxin tests performed during your accelerated stability studies in May 2000. Also, there were no real time stability studies conducted.**

11. **Your firm failed to conduct quarterly dose audits of your gamma radiation sterilization cycle as stated in your sterilization validation protocol dated 5/22/00.**

12. **Your firm failed to establish a protocol for periodic bioburden testing of the "Stripper."**

13. **Your firm failed to maintain procedures for identifying product during all stages of receipt, production, and distribution to prevent mixups. Records for lot 27800 show that [redacted] tips for the 125 micron size were received, [redacted] were sterilized, [redacted] were distributed and there is no quantity left in inventory. Discrepancies were also found with the 600 micron and 100 micron size tips for lot 27800 as well as with lot 35500.**

14. **Your firm failed to identify design inputs and design outputs, and perform a design review for their packaging design change of the "Stripper" pipette tips.**

15. **Your firm failed to establish and maintain quality requirements that must be met by contractors. For example, your firm failed to evaluate your contract sterility-testing laboratory.**

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued to you may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the cause of the violations identified by the Food and Drug Administration (FDA). If the causes are determined to be system problems, you must promptly initiate permanent corrective actions.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, requests for Certificates of Exportability to Foreign Governments will not be cleared until the violations related to the subject devices have been corrected.

You should take prompt measures to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction and/or civil penalties.

The agency is in receipt of your written response, dated March 8, 2001, to the FDA 483 issued to your firm on February 26, 2001. We acknowledge your firm's commitment to the Quality System Regulations; however, we need specific information about the corrective actions that your company has taken.

Please notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct these violations, including an explanation of each step taken to prevent their reoccurrence. Your response should include copies of any available documentation demonstrating that corrections have been made. If corrections cannot be completed within 15 working days, state the reason for the delay and the time frame within which the corrections will be completed. Your written reply should be directed to Diane B. Radice, Compliance Officer, FDA, 10 Waterview Blvd., Parsippany, NJ 07054.

Sincerely,

for DOUGLAS I. ELLSWORTH
DISTRICT DIRECTOR
New Jersey District